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(54) DIPHENYL AZETIDINONE DERIVATIVES
POSSESSING CHOLESTEROL ABSORPTION
INHIBITORY ACTIVITY

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(30) Foreign Application Priority Data

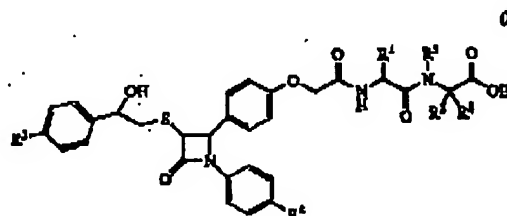
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(57) ABSTRACT

Compounds of formula (I) (wherein variable groups are as defined within) pharmaceutically acceptable salts, solvates, solvates of such salts and prodrugs thereof and their use as cholesterol absorption inhibitors for the treatment of hyperlipidaemia are described. Processes for their manufacture and pharmaceutical compositions containing them are also described.



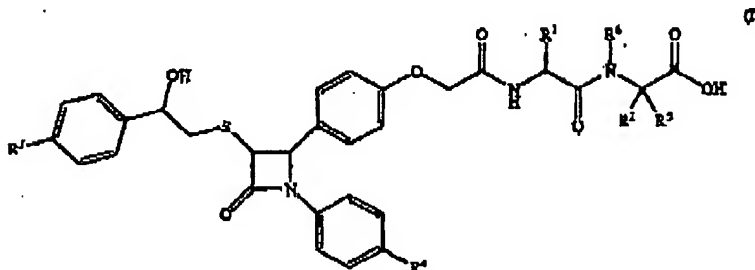
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continued	
Compound (I)	Caco Value (10 ³ cm/sec)
N-[4-[(2R,5R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl)phenoxy]-4-oxo-1,2,3,4-tetrahydropyrimidin-5-yl]-D-tyrosine	0.3
1-(4-fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethyl]-4-(R)-[4-[N-[(2-phenyl)-1-(R)-(carbamoyl)ethyl]carbamoylmethoxy]carbamoylmethoxy]pyrazole-2-one	0.09

1. A compound of formula (I):



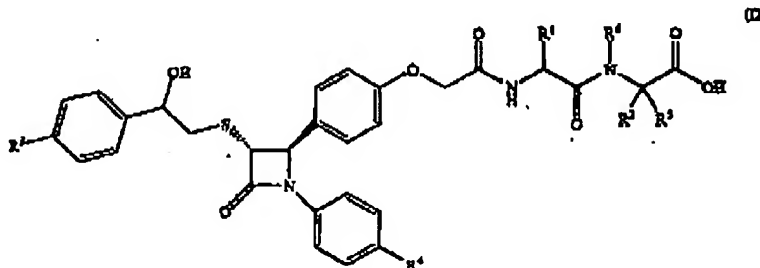
wherein:

R¹ is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl or aryl; wherein said C₁₋₆ alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆ alkoxy, N-(C₁₋₆ alkyl)amino, N,N-(C₁₋₆ alkyl)₂amino, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylS(O)_a, wherein a is 0-2, C₃₋₆ cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆ alkyl or C₁₋₆ alkoxy;
R² and R³ are independently hydrogen, a branched or unbranched C₁₋₆ alkyl, C₃₋₆ cycloalkyl or aryl; wherein said C₁₋₆ alkyl may be optionally substituted

aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆ alkyl or C₁₋₆ alkoxy;
R³ is hydrogen, alkyl, halo, C₁₋₆ alkoxy or C₁₋₆ alkyl;
R⁴ is hydrogen, C₁₋₆ alkyl, halo or C₁₋₆ alkoxy;
R⁵ is hydrogen, C₁₋₆ alkyl, or arylC₁₋₆ alkyl;
wherein R² and R³ may form a ring with 2-7 carbon atoms and wherein R⁴ and R⁵ may form a ring with 3-6 carbon atoms;
or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphonyl]-4-[4-(N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl]carbamoylmethoxy]phenyl]oxetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphonyl]-4-[4-(N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl]benzyl]carbamoylmethoxy]phenyl]oxetidin-2-one.

2. A compound of formula (II):



wherein:

R¹ is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl or aryl; wherein said C₁₋₆ alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆ alkoxy, N-(C₁₋₆ alkyl)amino,

by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆ alkoxy, aryl C₁₋₆ alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆ alkyl)amino, N,N-(C₁₋₆ alkyl)₂amino, C₁₋₆ alkylS(O)_a, C₃₋₆ cycloalkyl, aryl or aryl C₁₋₆ alkylS(O)_a, wherein a is 0-3; and wherein any

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N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylcarbonylamino, C₁₋₆alkylS(O)_a, wherein a is 0-2, C₂₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R³ and R² are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₂₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS-

R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁵ is hydrogen, C₁₋₆alkyl, or aryl C₁₋₆alkyl;

wherein R³ and R² may form a ring with 2-7 carbon atoms and wherein R⁴ and R⁵ may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphonyl]-4-[4-(N-[N-(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl)carbamoylmethoxy]phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphonyl]-4-[4-(N-(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl)benzyl]carbamoylmethoxy]phenyl]azetidin-2-one.

3. A compound according to claim 1, wherein:

R¹ is hydrogen or phenyl.

4. A compound according to claim 1, wherein:

R² is hydrogen, a branched or unbranched C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, acylamino,

C₁₋₆alkylS(O)_a, wherein a is 0-2, C₂₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

5. A compound according to claim 1, wherein:

R³ is hydrogen, C₁₋₆alkyl, halo or methoxy.

6. A compound according to claim 1, wherein:

R³ is hydrogen, methyl, chlorine, fluorine, C₁₋₆alkylS or methoxy.

7. A compound according to claim 1, wherein:

R⁴ is hydrogen or halo.

8. A compound according to claim 1, wherein:

R⁴ is chlorine or fluorine.

9. A compound according to claim 1, wherein:

R⁴ is hydrogen, C₁₋₆alkyl, aryl C₁₋₆alkyl or R⁴ and R⁵ form a ring with 3-6 carbon atoms.

10. A compound according to claim 1, wherein:

R¹ is hydrogen;

R² is a branched or unbranched C₁₋₆alkyl, optionally substituted by a C₂₋₆cycloalkyl, alkylS-, aryl optionally substituted by hydroxy or cyano, amino, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2;

R³ and R⁴ are halo;

R⁵ is hydrogen or C₁₋₆alkyl; and

R⁶ is hydrogen.

11. One or more compounds chosen from:

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-N⁶-acetyl-D-lysine;

1-(4-fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-[4-[N-[N-[2-(phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl]carbamoylmethoxy]phenyl]azetidin-2-one;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-D-valine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-D-tyrosine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-D-proline;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-D-lysine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-hydroxy-2-(4-methoxyphenyl)ethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-D-valine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-2-butylthiouracine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-3-methyl-L-cysteine;

N-[(4-(2R,3R)-1-(4-chlorophenyl)-3-[(2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-3-cyclohexyl-D-alanine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-3-cyclohexyl-D-alanine;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]glycyl-4-methyl-L-proline;

N-[(4-(2R,3R)-1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxazetidin-2-yl]phenoxy]acetyl]-L-alanyl-D-valine;

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N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-hydroxy-2-(4-methylphenyl)ethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-D-valine;

N-[[4-((2R,3R)-1-(4-chlorophenyl)-3-([2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-D-valine;

N-[[4-((2R,3R)-1-(4-chlorophenyl)-3-([2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-methyl-D-valine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-(2-naphthyl)-D-alanine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-methyl-D-valine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-(4S,5R)-3,4,5,6-tetrahydroxy-D-norleucine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-N,2-dimethylalanine;

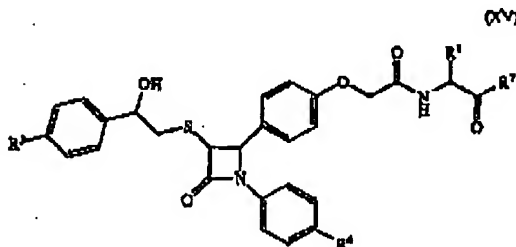
N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-methyl-D-valine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-S-(4-methylbenzyl)-D-cysteine;

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-S-(tert-butyl)-D-cysteine; and

N-[[4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-bis-(dimethyl-D-phenylalanine).

12. A compound of the formula (XV) or hydrolysable esters or amides thereof:



wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylcarboxy-

lamino, C₁₋₆alkylS(O)_n, wherein n is 0-2, C₁₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_n, C₁₋₆alkylS(C₁₋₆alkyl) wherein n is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R⁴ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS-;

R⁵ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl, or arylC₁₋₆alkyl; and

R⁷ is an hydroxy group or a C₁₋₃alkoxy group;

wherein R² and R³ may form a ring with 2-7 carbon atoms and wherein R⁴ and R⁵ may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphenyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphenyl]-4-[4-(N-{(R)-α-[N-[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl]benzyl}carbamoylmethoxy)phenyl]azetidin-2-one.

13. A method of treating or preventing a hyperlipidemic condition comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

14. A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

15. A method for treating or preventing Alzheimer's disease comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

16. A method for treating or preventing a cholesterol associated tumor comprising the administration of an effective amount of a compound according to claim 1 to a mammal in need thereof.

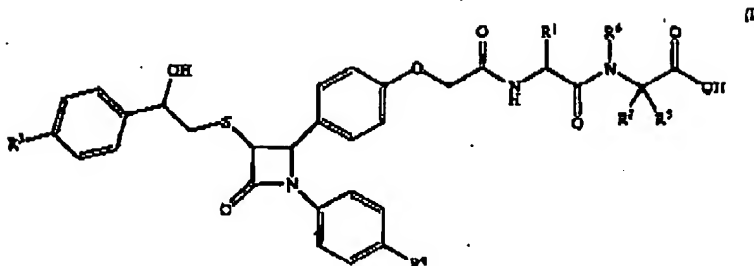
17. A pharmaceutical formulation comprising a compound according to claim 1 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier.

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15. A combination of a compound according to formula (1)



wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₂₋₆alkylcarbamoylamino, C₂₋₆alkylS(O)_a, wherein a is 0-2, C₂₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

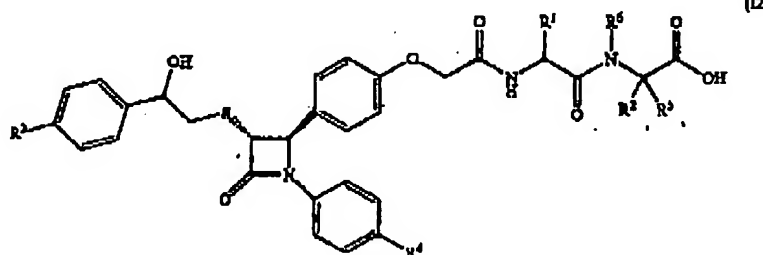
R² and R³ are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl,

carboxy, C₁₋₆alkoxy, aryl, C₁₋₆alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₂₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy; R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS—;

R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁵ is hydrogen, C₁₋₆alkyl or aryl(C₁₋₆alkyl); wherein R² and R³ may form a ring with 2-7 carbon atoms and wherein R⁴ and R⁵ may form a ring with 3-6 carbon atoms;

or according to formula (12)



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wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl;
wherein said C₁alkyl may be optionally substituted
by one or more hydroxy, amino, guanidino, carbam-
oyl, carboxy, C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino,
N,N-(C₁₋₆alkyl)carbamoyl, C₁₋₆alkylS(O)_a,
wherein a is 0-2, C₂₋₆cycloalkyl or aryl; and wherein
any aryl group may be optionally substituted by one
or two substituents selected from halo, hydroxy,
C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R³ are independently hydrogen, a branched or
unbranched C₁₋₆alkyl

C₂₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be
optionally substituted by one or more hydroxy, amino,
guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy,
aryl, C₁₋₆alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆alkyl)amino, N,N-
(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₂₋₆cycloalkyl,
aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and
wherein any aryl group may be optionally substituted
by one or two substituents selected from halo, hydroxy,
C₁₋₆alkyl or C₁₋₆alkoxy;

R⁴ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆
alkylS

R⁵ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl or aryl; C₁₋₆alkyl

wherein R³ and R² may form a ring with 2-7 carbon atoms
and wherein R⁶ and R⁵ may form a ring with 3-6 carbon
atoms;

with a PPAR alpha and/or gamma agonist.

19. A combination of a compound according to formula
(1)

wherein:

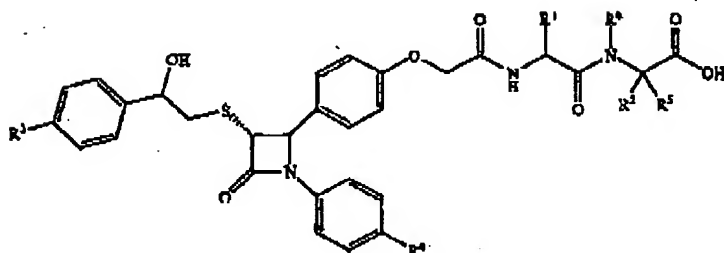
R¹ is hydrogen, C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl;
wherein said C₁alkyl may be optionally substituted
by one or more hydroxy, amino, guanidino, carbam-
oyl, carboxy, C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino,
N,N-(C₁₋₆alkyl)carbamoyl, C₁₋₆alkylS(O)_a,
wherein a is 0-2, C₂₋₆cycloalkyl or aryl; and wherein
any aryl group may be optionally substituted by one
or two substituents selected from halo, hydroxy,
C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R³ are independently hydrogen, a branched or
unbranched C₁₋₆alkyl, C₂₋₆cycloalkyl or aryl; wherein
said C₁₋₆alkyl may be optionally substituted by one or
more hydroxy, amino, guanidino, cyano, carbamoyl,
carboxy, C₁₋₆alkoxy, aryl, C₁₋₆alkoxy, (C₁₋₆)₂Si,
N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino,
C₁₋₆alkylS(O)_a, C₂₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS
(O)_a, wherein a is 0-2; and wherein any aryl group may
be optionally substituted by one or two substituents
selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;
R⁴ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆
alkylS

R⁵ is hydrogen, C₁₋₆alkyl halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl, or aryl; C₁₋₆alkyl

wherein R³ and R² may form a ring with 2-7 carbon atoms
and wherein R⁶ and R⁵ may form a ring with 3-6 carbon
atoms;

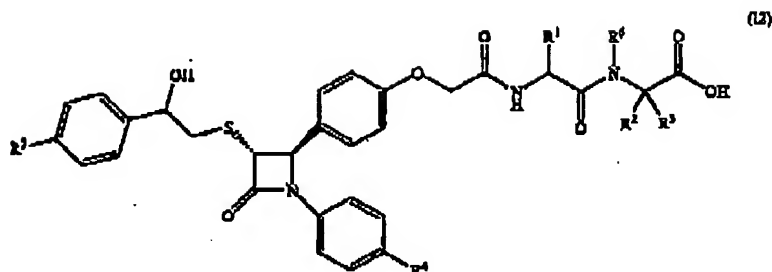


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or according to formula (12)



wherein:

$\rightarrow C_{1-6}$ \rightarrow R^1 is hydrogen, C_{1-6} alkyl, C_{2-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C_{1-6} alkoxy, $N-(C_{1-6}$ alkyl)amino, $N,N-(C_{1-6}$ alkyl)₂amino, C_{1-6} alkylcarbamoylamino, C_{1-6} alkylS(O)_n wherein n is 0-2, C_{2-6} cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

$\rightarrow C_{1-6}$ \rightarrow R^2 and R^3 are independently hydrogen, a branched or unbranched C_{1-6} alkyl, C_{2-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6} alkoxy, aryl, C_{1-6} alkoxy, $(C_{1-6})_2$ Si, $N-(C_{1-6}$ alkyl)amino, $N,N-(C_{1-6}$ alkyl)₂amino, C_{1-6} alkylS(O)_n, C_{2-6} cycloalkyl, aryl or aryl C_{1-6} alkylS(O)_n wherein n is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

$\rightarrow R^5$ \rightarrow R^3 is hydrogen, alkyl, halo, C_{1-6} alkoxy or C_{1-6} alkylS -;

$\rightarrow R^5$ \rightarrow R^4 is hydrogen, C_{1-6} alkyl halo or C_{1-6} alkoxy;

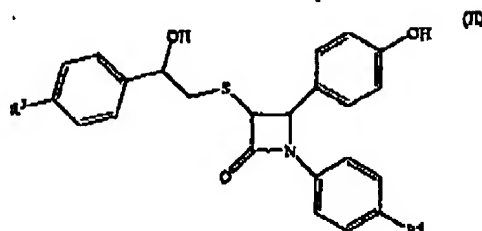
$\rightarrow R^5$ \rightarrow R^6 is hydrogen, C_{1-6} alkyl or aryl(C_{1-6} alkyl);

$\rightarrow R^5$ \rightarrow wherein R^5 and R^7 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a ring with 3-6 carbon atoms;

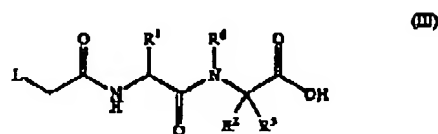
with an HMG Co-A reductase inhibitor.

20. A process for preparing a compound or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof comprising:

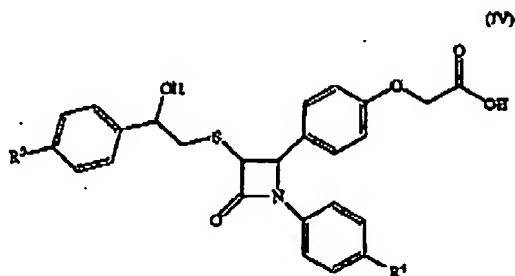
a) reacting a compound of formula (II):



with a compound of formula (III):



b) reacting an acid of formula (IV):



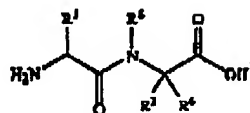
or an activated derivative thereof;

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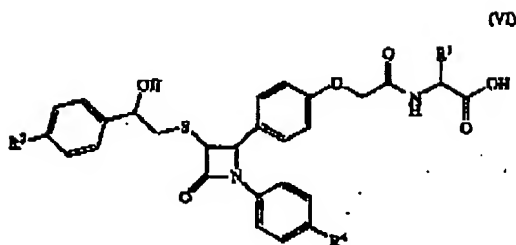
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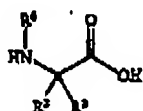
with an amine of formula (V):



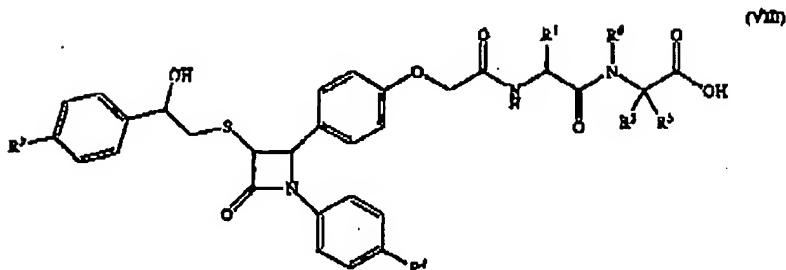
c) reacting an acid of formula (VI):



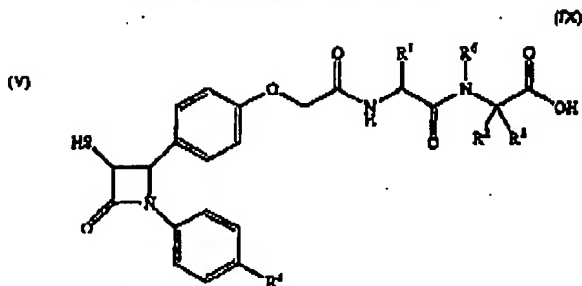
or an activated derivative thereof, with an amine of formula (VII):



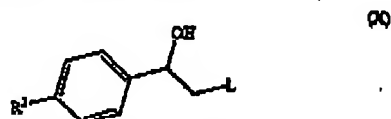
d) reducing a compound of formula (VIII):



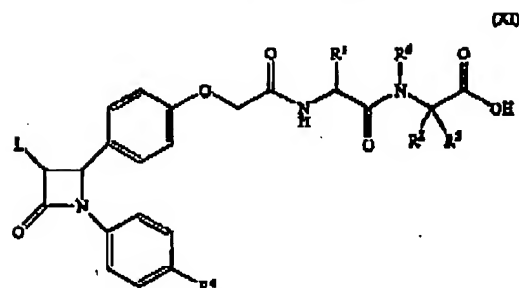
e) reacting a compound of formula (IX):



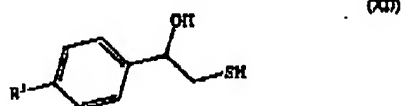
with a compound of formula (X):



f) reacting a compound of formula (XI):



with a compound of formula (XII):

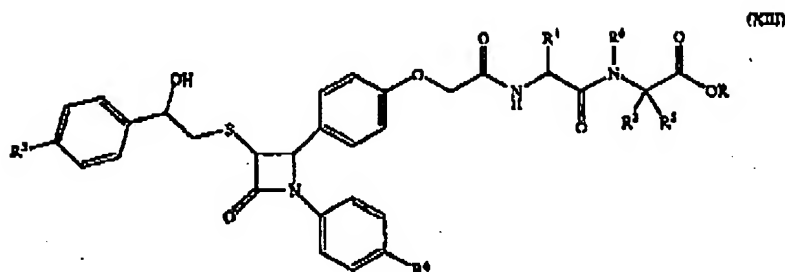


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g) De-esterifying a compound of formula (XIII)



wherein the group C(O)OR is an ester group; and
wherein:

R¹ is hydrogen, C₁₋₆ alkyl, C₂₋₆ cycloalkyl or aryl; wherein said C₁₋₆ alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆ alkoxy, N-(C₁₋₆ alkyl)amino, N,N-(C₁₋₆ alkyl)₂amino, C₁₋₆ alkylcarbonylamino, C₁₋₆ alkylS(O)_n, wherein n is 0-2, C₂₋₆ cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆ alkyl or C₁₋₆ alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C₁₋₆ alkyl, C₂₋₆ cycloalkyl or aryl; wherein said C₁₋₆ alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆ alkoxy, aryl C₁₋₆ alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆ alkyl)amino, N,N-(C₁₋₆ alkyl)₂amino, C₁₋₆ alkylS(O)_n, C₂₋₆ cycloalkyl aryl or aryl C₁₋₆ alkylS(O)_n, wherein n is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆ alkyl, or C₁₋₆ alkoxy;

R⁴ is hydrogen, alkyl, halo, C₁₋₆ alkoxy or C₁₋₆ alkylS-; R⁵ is hydrogen, C₁₋₆ alkyl, halo or C₁₋₆ alkoxy; R⁶ is hydrogen, C₁₋₆ alkyl or aryl(C₁₋₆ alkyl); wherein R⁵ and R⁶ may form a ring with 2-7 carbon atoms and wherein R⁶ and R⁷ may form a ring with 3-6 carbon atoms; and

L is a displaceable group; and thereafter optionally:

- converting a compound of the formula (I) into another compound of the formula (I);
- removing any protecting groups;

- forming a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug; or
- separating two or more enantiomers.

21. A method of treating or preventing a hyperlipidemic condition comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

22. A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

23. A method for treating or preventing Alzheimer's disease comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

24. A method for treating or preventing a cholesterol associated tumor comprising the administration of an effective amount of a compound according to claim 12 to a mammal in need thereof.

25. A pharmaceutical formulation comprising a compound according to claim 12 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier.

26. A process according to claim 20 wherein L is a halogen or sulphonyloxy group.

27. A process according to claim 26 wherein L is a chloro, bromo, methanesulphonyloxy or toluene-4-sulphonyloxy group.

28. A process according to claim 20 wherein the C(O)OR ester group is methoxycarbonyl, ethoxycarbonyl, t-butoxycarbonyl, or benzyloxycarbonyl.

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Preliminary Amendment.

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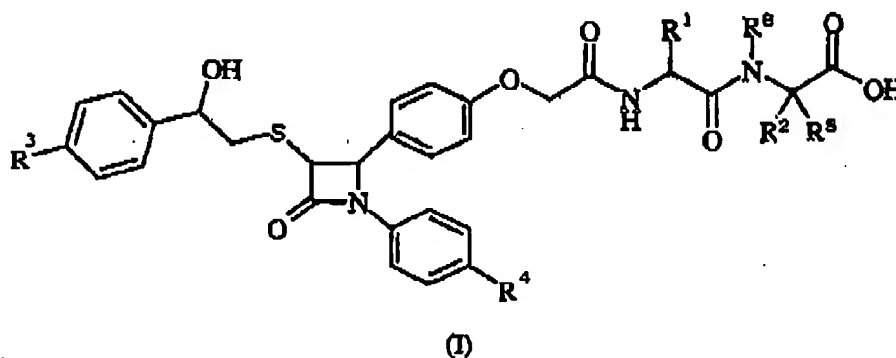
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In the Claims:

The current status of all claims is listed below and supercedes all previous lists of claims.

Please amend claims 1-20, and add new claims 21-28 as follows.

1. (currently amended) A compound of formula (I):



wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkylcarbamoylamino, C₁₋₆alkylcarboxylamino, C₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R⁵ are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆)₃Si, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₁₋₆alkylS(O)_a, C₃₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS-

R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl, or arylC₁₋₆alkyl;

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or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug

→ fluorophenyl]-2-hydroxyethylsulphonyl]-4-[4-(N-[N-(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl)carbamoylmethoxy]phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphonyl]-4-[4-(N-(R)- α -(N-[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl)benzyl)carbamoylmethoxy]phenyl]azetidin-2-one.

The chemical structure shows a penicillin core. The 6-aminopenicillanic acid moiety is substituted at the 6-position with a side chain: $-CH_2-S-CH(OH)-C_6H_4-R^3$. The 4-position of the penicillin core is substituted with a phenyl group bearing a substituent R^4 . The 2-position of the penicillin core is substituted with a side chain: $-CH_2-O-CO-NH-CH(R^1)-CO-N(R^2)(R^5)-C(R^6)(R^7)-COOH$.

(12)

R¹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, *N*-(C₁₋₆alkyl)amino, *N,N*-(C₁₋₆alkyl)₂amino, C₁₋₆alkylcarbamoylamino, C₁₋₆alkylcarboxylamino, C₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6} alkoxy, aryl C_{1-6} alkoxy, $(C_{1-4})_3Si$, $N-(C_{1-6}alkyl)amino$, $N,N-(C_{1-6}alkyl)_2amino$, $C_{1-6}alkylS(O)_2$, $C_{1-6}alkylS(O)_2C_{3-6}cycloalkyl$, aryl or

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aryl C₁₋₆ alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆ alkylS-

R⁴ is hydrogen, C₁₋₆ alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆ alkyl, or arylC₁₋₆ alkyl;

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R³ may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-((R)-α)-{N-[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl)carbamoylmethoxy]phenyl]azetidin-2-one.

3. (currently amended) A compound according to claim 1 or 2, wherein:

R¹ is hydrogen or phenyl.

4. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R² is hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, acylamino,

C₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by hydroxy, alkyl, alkoxy or cyano.

5. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R³ is hydrogen, C₁₋₆alkyl, halo or methoxy.

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6. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^3 is hydrogen, methyl, chlorine, fluorine, C_{1-6} alkylS-, or methoxy.

7. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^4 is hydrogen or halo,

8. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^4 is chlorine or fluorine.

9. (currently amended) A compound according to ~~any of the preceding claims~~ claim 1, wherein:

R^6 is hydrogen, C_{1-6} alkyl, aryl C_{1-6} alkyl or R^6 and R^2 form a ring with 3-6 carbon atoms.

10. (currently amended) A compound according to claim 1, wherein:

R^1 is hydrogen;

R^2 is a branched or unbranched C_{1-6} alkyl, optionally substituted by a C_{3-6} cycloalkyl, alkylS-, aryl optionally substituted by hydroxy or cyano, amino, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino or aryl C_{1-6} alkylS(O)_n, wherein n is 0-2 0-2;

R^3 and R^4 are halo;

R^5 is hydrogen or C_{1-6} alkyl; and

R^6 is hydrogen.

11. (currently amended) One or more compounds chosen from:

N -{[4-($(2R,3R)$ -1-(4-fluorophenyl)-3-[(2-(4-fluorophenyl)-2-hydroxyethyl)thio]-4-oxoazetidin-2-yl)phenoxy]acetyl}glycyl- N^6 -acetyl-D-lysine;

1-(4-fluorophenyl)-3-(R)-[2-(4-fluorophenyl)-2-hydroxyethylthio]-4-(R)-[4-[N -[N -[2-

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(phenyl)-1-(R)-(carboxy)ethyl]carbamoylmethyl]carbamoylmethoxy]phenyl]azetidin-2-one;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-valine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-tyrosine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-proline;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-lysine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-hydroxy-2-(4-methoxyphenyl)ethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-valine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-2-butyl-L-leucine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-S-methyl-L-cysteine;
N-([4-((2R,3R)-1-(4-chlorophenyl)-3-([2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-3-cyclohexyl-D-alanine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-3-cyclohexyl-D-alanine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-4-methyl-L-leucine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)-L-alanyl-D-valine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-hydroxy-2-(4-methylphenyl)ethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-valine;
N-([4-((2R,3R)-1-(4-chlorophenyl)-3-([2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-D-valine;
N-([4-((2R,3R)-1-(4-chlorophenyl)-3-([2-(4-chlorophenyl)-2-hydroxyethyl]thio)-4-oxoazetidin-2-yl)phenoxy]acetyl)glycyl-3-methyl-D-valine;
N-([4-((2R,3R)-1-(4-fluorophenyl)-3-([2-(4-fluorophenyl)-2-hydroxyethyl]thio)-4-

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oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-(2-naphthyl)-D-alanine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-methyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-(3*R*,4*S*,5*R*)-3,4,5,6-tetrahydroxy-D-norleucine;
norleucine;

N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-*N*,2-dimethylalanine dimethylalanine;

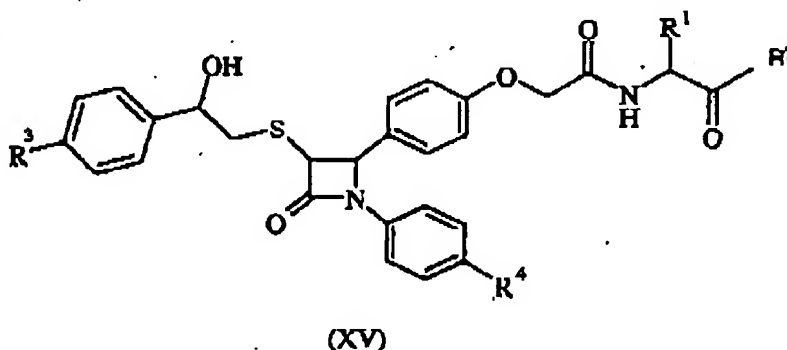
N-{[4-((2*R*,3*R*)-1-(4-Fluorophenyl)-3-[[2-hydroxy-2-[4-(methylthio)phenyl]ethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-3-methyl-D-valine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-S-(4-methylbenzyl)-D-cysteine cysteine;

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-S-(*tert*-butyl)-D-cysteine cysteine; and

N-{[4-((2*R*,3*R*)-1-(4-fluorophenyl)-3-[[2-(4-fluorophenyl)-2-hydroxyethyl]thio]-4-oxoazetidin-2-yl)phenoxy]acetyl]glycyl-b,b-dimethyl-D-phenylalanine.

12. (currently amended) A compound of the formula (XV) or hydrolysable esters or amides thereof:



wherein:

*R*¹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be

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optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy,
 → C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₂₋₆alkylcarbamoylamine, C₁₋₆alkylcarbamoylamino, C₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R³ are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆)₂Si, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, or C₁₋₆alkylS(O)_a, arylC₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS-;

R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl, or arylC₁₋₆alkyl; and

R⁷ is an hydroxy group or a C₁₋₃alkoxy group;

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms;

or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof;

with the proviso that said compound is not 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-{N-[(R)-1-(carboxy)-2-(hydroxy)ethyl]carbamoylmethyl}carbamoylmethoxy)phenyl]azetidin-2-one; or 3-(R)-4-(R)-1-(phenyl)-3-[2-(4-fluorophenyl)-2-hydroxyethylsulphanyl]-4-[4-(N-[(R)-α-{N-[(S)-1-(carboxy)-2-(hydroxy)ethyl]carbamoyl}benzyl}carbamoylmethoxy)phenyl]azetidin-2-one.

13. (currently amended) A method of treating or preventing a hyperlipidemic condition hyperlipidemic conditions comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 claim 1 to a mammal in need thereof.

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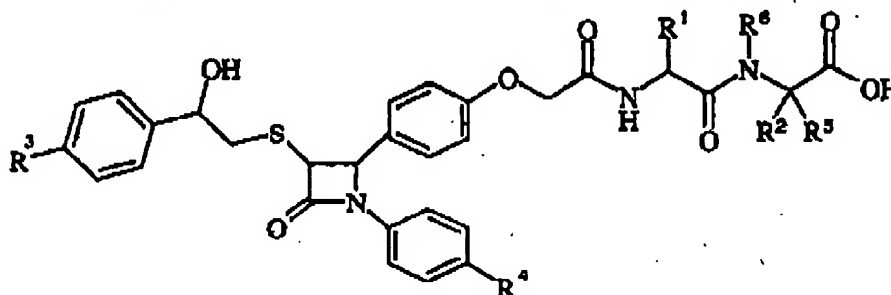
14. (currently amended) A method of treating or preventing atherosclerosis comprising the administration of an effective amount of a compound according to any one of claims 1 to 12 claim 1 to a mammal in need thereof.

15. (currently amended) A method for treating or preventing Alzheimers' disease comprising the administration of an effective amount of a compound according to any one of ~~claims 1 to 12~~ claim 1 to a mammal in need thereof.

16. (currently amended) A method for treating or preventing a cholesterol associated tumor ~~cholesterol-associated tumors~~ comprising the administration of an effective amount of a compound according to ~~any one of claims 1 to 12~~ claim 1 to a mammal in need thereof.

17. (currently amended) A pharmaceutical formulation comprising a compound according to ~~any one of claims 1 to 12~~ claim 1 in admixture with a pharmaceutically acceptable adjuvant, diluent and/or carrier, ~~adjuvants, diluents and/or carriers.~~

18. (currently amended) A combination of a compound according to formula (I)



II

wherein:

R¹ is hydrogen, C₁-alkyl, C₃-cycloalkyl or aryl; wherein said C₁-alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy, C₁-alkoxy, N-(C₁-alkyl)amino, N,N-(C₁-alkyl)amino, C₁-C₆ alkylcarbonamino, C₁-alkylS(O)_a, wherein a is 0-2, C₃-cycloalkyl or aryl; and wherein any aryl group may be

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optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl orC₁₋₆alkoxy;

R² and R⁵ are independently hydrogen, a branched or unbranched C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C₁₋₆alkoxy, aryl C₁₋₆alkoxy, (C₁₋₆)₃Si, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylS(O)_a, C₃₋₆cycloalkyl, aryl or aryl C₁₋₆alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

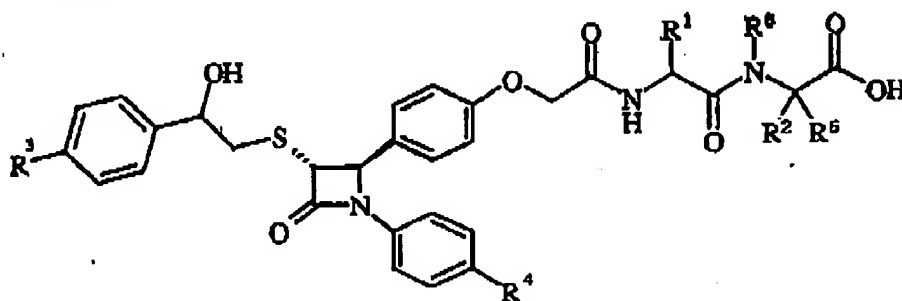
R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkylS-

R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;

R⁶ is hydrogen, C₁₋₆alkyl, or arylC₁₋₆alkyl;

wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R² may form a ring with 3-6 carbon atoms;

or according to formula (I2)



(I2)

wherein:

R¹ is hydrogen, C₁₋₆alkyl, C₃₋₆cycloalkyl or aryl; wherein said C₁₋₆alkyl may be optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy,

C₁₋₆alkoxy, N-(C₁₋₆alkyl)amino, N,N-(C₁₋₆alkyl)₂amino, C₁₋₆alkylcarbonylamino, C₁₋₆alkylS(O)_a, wherein a is 0-2, C₃₋₆cycloalkyl or aryl; and wherein any aryl group may be optionally substituted by one or two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;

R² and R⁵ are independently hydrogen, a branched or unbranched C₁₋₆alkyl,

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with a PPAR alpha and/or gamma agonist.

OC(=O)C(R2)(R5)N(R6)C(=O)NC(=O)COc1ccc(cc1)C23C(=O)N(c4ccc(cc4)R4)C(=O)S2Cc5ccc(cc5)R3O

Q

C₂-cycloalkyl or aryl; wherein said C₁-alkyl may be optionally substituted by one or more

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hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6} alkoxy, aryl C_{1-6} alkoxy, $(C_{1-6})_3Si$,
→ N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a, C_{3-6} cycloalkyl, aryl or aryl C_{1-6}
alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or
two substituents selected from halo, hydroxy, C_{1-6} alkyl or C_{1-6} alkoxy;

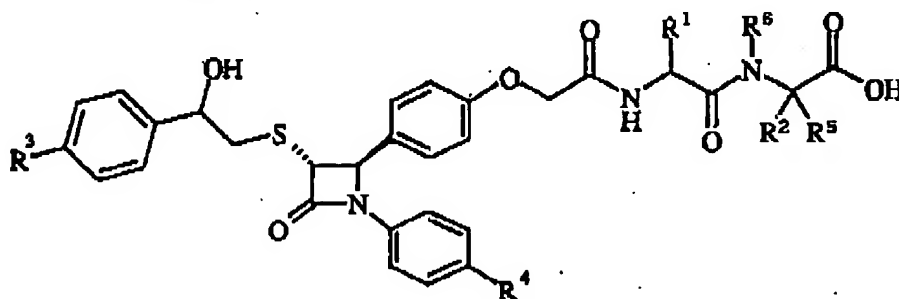
R^3 is hydrogen, alkyl, halo, C_{1-6} alkoxy or C_{1-6} alkylS-;

R^4 is hydrogen, C_{1-6} alkyl, halo or C_{1-6} alkoxy;

R^6 is hydrogen, C_{1-6} alkyl, or aryl C_{1-6} alkyl;

wherein R^5 and R^2 may form a ring with 2-7 carbon atoms and wherein R^6 and R^2 may form a
ring with 3-6 carbon atoms;

or according to formula (I2)



(I2)

wherein:

R^1 is hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be
optionally substituted by one or more hydroxy, amino, guanidino, carbamoyl, carboxy,
 C_{1-6} alkoxy, N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylcarbonylamino,
 C_{1-6} alkylS(O)_a, wherein a is 0-2, C_{3-6} cycloalkyl or aryl; and wherein any aryl group may be
optionally substituted by one or two substituents selected from halo, hydroxy, C_{1-6} alkyl or
 C_{1-6} alkoxy;

R^2 and R^5 are independently hydrogen, a branched or unbranched C_{1-6} alkyl,
 C_{3-6} cycloalkyl or aryl; wherein said C_{1-6} alkyl may be optionally substituted by one or more
hydroxy, amino, guanidino, cyano, carbamoyl, carboxy, C_{1-6} alkoxy, aryl C_{1-6} alkoxy, $(C_{1-6})_3Si$,
→ N -(C_{1-6} alkyl)amino, N,N -(C_{1-6} alkyl)₂amino, C_{1-6} alkylS(O)_a, C_{3-6} cycloalkyl, aryl or aryl C_{1-6}
alkylS(O)_a, wherein a is 0-2; and wherein any aryl group may be optionally substituted by one or

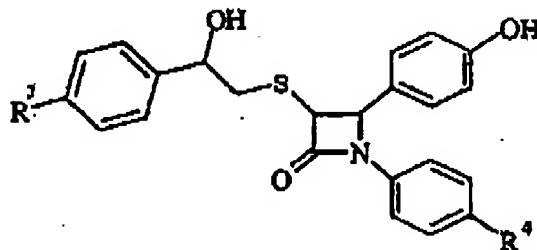
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two substituents selected from halo, hydroxy, C₁₋₆alkyl or C₁₋₆alkoxy;R³ is hydrogen, alkyl, halo, C₁₋₆alkoxy or C₁₋₆alkyl;R⁴ is hydrogen, C₁₋₆alkyl, halo or C₁₋₆alkoxy;R⁶ is hydrogen, C₁₋₆alkyl, or arylC₁₋₆alkyl;wherein R⁵ and R² may form a ring with 2-7 carbon atoms and wherein R⁶ and R³ may form a ring with 3-6 carbon atoms;

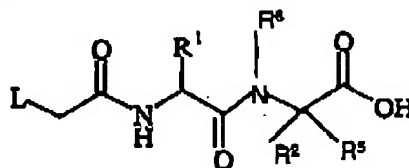
with an HMG Co-A reductase inhibitor.

20. (currently amended) A process for preparing a compound of formula (I) or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof which process (wherein variable groups are, unless otherwise specified, as defined in formula (I)) comprises of comprising:

Process-1) a) reacting a compound of formula (II):

(II)

with a compound of formula (III):



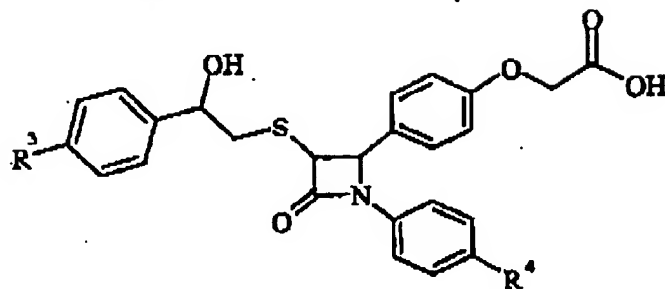
(III)

wherein L is a displaceable group;

Process-2) b) reacting an acid of formula (IV):

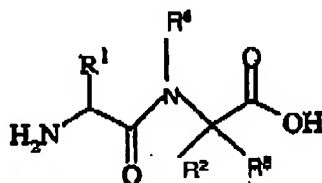
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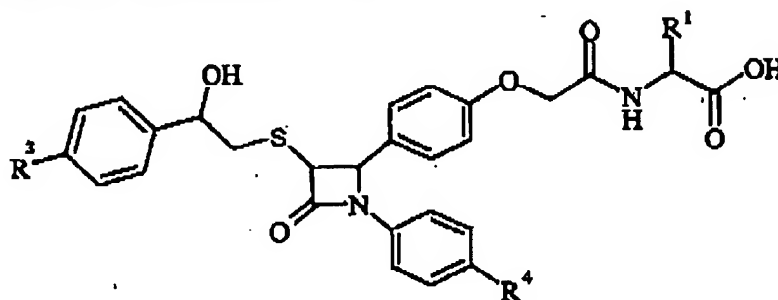
(IV)

or an activated derivative thereof;
with an amine of formula (V):



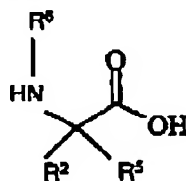
(V)

Process 3): c) reacting an acid of formula (VI):



(VI)

or an activated derivative thereof, with an amine of formula (VII):



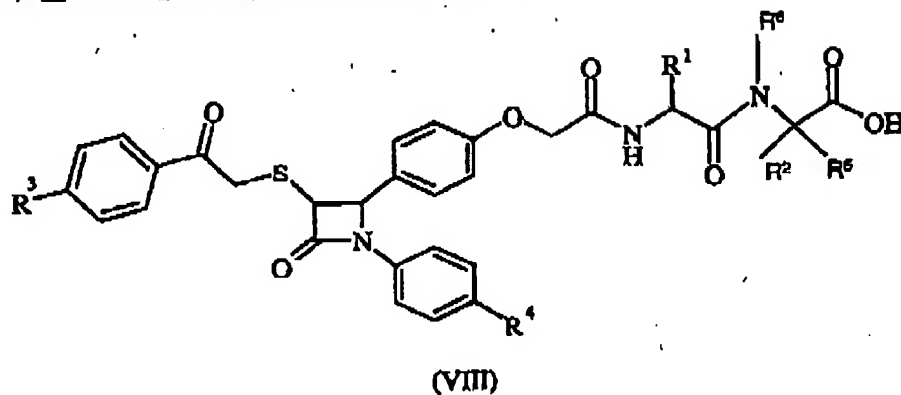
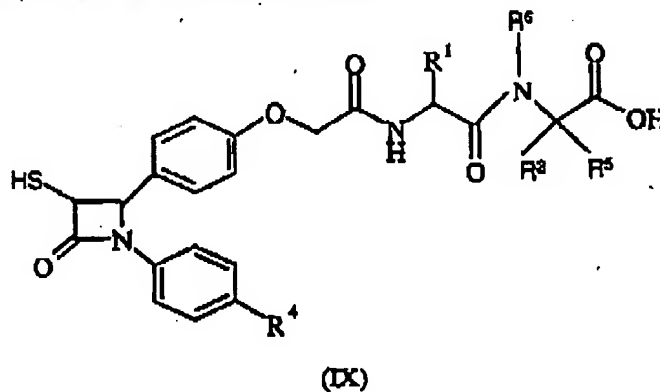
(VII)

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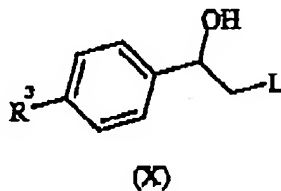
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~~Process 4:~~ d) reducing a compound of formula (VIII):~~Process 5:~~ e) reacting a compound of formula (IX):

with a compound of formula (X):



wherein L is a displacable group;

~~Process 6:~~ f) reacting a compound of formula (XI):